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Hyperuricemia in psoriatic arthritis: prevalence and associated factors

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ABSTRACT

Hyperuricemia is frequent in psoriatic arthritis (PsA) and it seems to be related to metabolic syndrome rather than extensive psoriatic skin disease. The objectives of this study were to evaluate the prevalence of hyperuricemia in PsA patients and to identify the associ-ated factors.

Design: cross-sectional study, including consecutive, unselected, adult PsA patients. Data collection: demographic variables (age, gender, disease duration), clinical variables (affected joints, current moderate/severe psoriasis, nail disease, axial involvement, enthesi-tis, dactylitis), laboratory variables (acute phase reactants), treatment-related variables (non-steroidal anti-inflammatory drugs, corticosteroids, synthetic and biologic disease modifying drugs) and comorbidities. Hyperuricemia was defined as uric acid level above 6.8 mg/dl. Statistical analysis: the factors that were potentially associated with hyperuricemia were assessed by uni- and multivariate logistic regression.

In all, 120 PsA patients were included in the study: 69 (57.5%) women, mean age±standard deviation 54±11.8 years, mean disease duration 7±7.4 years; 24 (20%) had moderate/severe psoriasis and 30 (25%) were taking a biologic. Around a quarter of patients had hyperuricemia (33; 27.5%). Hyperuricemia was significantly associated with obesity, diabetes, ischemic heart disease and hypertension, but there was no correlation with current skin psoriasis. In the multivariate analysis, it was best explained by diabetes (odds ratio: 4.95, [95% confidence intervals: 1.47; 16.67]), ischemic heart disease (3.61 [1.00; 12.98]) and obesity (1.86 [1.04; 3.32]).

Hyperuricemia in PsA is associated with metabolic syndrome rather than skin dis-ease, but further longitudinal studies are needed to identify causal relationships.

Keywords: psoriatic arthritis, hyperuricemia, moderate/severe psoriasis, metabolic syndrome

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disease which is associated with skin psoriasis. Studies have demonstrated associations between PsA and multiple comorbidities, in particular cardiovascular risk factors and diseases (1-5). Although little studied, the relationship between PsA and hyperuricemia is well-known for a long time (6). The prevalence of hyperuricemia in PsA is reported to be around 20% (7) and the main proposed cause was the extension of psoriasis lesions, through an increased cellular turn-over (8). However, more recent studies have suggested that hyperuricemia in PsA and in psoriasis also is due to the association with the metabolic syndrome and cardiovascular comorbidities, in particular obesity and hyperlipidaemia (7, 9-11).

The objective of this study was to evaluate the prevalence of hyperuricemia in PsA patients and to identify the associated factors.

METHODS

Study design and patients

The study had a cross-sectional design and included unselected, consecutive adult patients with definite PsA according to the physician, with a range of disease manifestations and treatments. Most of them fulfilled the CASPAR classification criteria for PsA [12]. All patients gave a written informed con-

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sent and the protocol of the study was approved by the local ethics committee.

Data collection

Several variables, i.e., demographic, clinical, laboratory variables and data on comorbidities and treatment were collected. Demographic features included age, gender and disease duration. Disease-related characteristics included swollen joint count, SJC (0-66), tender joint count, TJC (0-68), current moderate or severe psoriasis, i.e., more than 5% body surface, nail disease, other activity such as dactylitis, enthesitis and axial involvement, and acute phase reactants, e.g., C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Data regarding treatment included current and past non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, synthetic and biologic disease modifying drugs (sDMARDs, b DMARDs, respectively). Data on comorbidities were also collected, according to the recent European League Against Rheumatism (EULAR) recommendations on reporting, screening and preventing comorbidities in chronic inflammatory rheumatic diseases (13). This included cardiovascular diseases (i.e., history of myocardial infarction, pectoris angina, stent, stroke, transient ischemic attack, heart failure and lower limb peripheral arterial disease), malignancies (i.e., any history of malignancy), infections (i.e., history of tuberculosis, of serious infections, opportunistic infections and chronic viral infections), gastro-intestinal diseases (i.e., history of peptic ulcer), osteoporosis and depression. Risk factors and current treatment for comorbid conditions were also collected.

Statistical analysis

Hyperuricemia was defined as serum uric acid level above 6.8 mg/dl (14) since it was shown that this level defines the saturation point of the sodium urate salt in biologic fluids at physiologic pH and temperature (15).

Associations between hyperuricemia and other variables were tested by Spearman's correlation (statistical significance: $p<0.05$). Factors associated to hyperuricemia were identified by performing univariate and multivariate logistic regressions. The variables tested were: age, gender, disease duration, SJC, TJC, CRP, ESR, current moderate/sever psoriasis, nail disease, other activity (dactylitis, enthesitis, axial involvement), current NSAIDs, corticosteroids, sDMARDs and bDMARDs and comorbidities and risk factors, as described above. Only variables that were statistically significant associated to hyperuricemia in the univariate logistic regression ($p<0.10$) were included in the multivariate analysis.

There was no imputation of missing data. Statistics were performed using SPPS for IBM, version 20.0.

RESULTS

Patient characteristics

A total of 120 PsA patients were analysed (Table 1). Mean±standard deviation age was 54±11.8 years,

TABLE 1. *Characteristics of 120 patients with psoriatic arthritis, according to the presence of hyperuricemia*

Patient characteristics	All patients (N=120)	Patients with hyperuricemia (N=33)	Patients with normouricemia (N=87)
Females, N (%)	69 (57.5)	15 (45.5)	54 (62)
Age, years, mean (SD)	54 (11.8)	56.5 (10.9)	53.1 (12.1)
PsA disease duration, years, mean (SD)	7.2 (7.5)	5.5 (5.7)	7.8 (8.1)
Swollen joint count (0-66), median (range)	0 (0, 9)	0 (0, 4)	0 (0, 9)
Tender joint count (0-68), median (range)	2 (0, 22)	2 (0, 14)	2 (0, 22)
CRP, mg/L, median (range)	7 (0, 121)	6.5 (0, 65)	7.4 (0, 21)
Current moderate/ severe skin psoriasis, N (%)	24 (20)	7 (29.2)	17 (70.8)
Enthesitis, N (%)	18 (15)	7 (38.9)	11 (61.1)
Dactylitis, N (%)	31 (25.8)	8 (25.8)	23 (74.2)
Obesity, N (%)	41 (34.2)	18 (54.5)	23 (26.4)
Hypertension, N (%)	62 (51.7)	22 (66.7)	40 (46.5)
Diabetes, N (%)	18 (15)	11 (33.3)	7 (8.0)
Ischemic heart disease, N (%)	15 (12.5)	8 (4.22)	7 (8.0)
Biologic drug, N (%)	30 (25)	8 (26.7)	22 (73.3)

SD: standard deviation; PsA: psoriatic arthritis; CRP: C-reactive protein

mean disease duration was 7.2±7.5 years and the majority were females (57.5%). Twenty four patients (20%) presented current moderate/severe skin psoriasis. Most of them (78.3%) were treated with a synthetic DMARD and about a quarter (25%) with a biologic drug. Many patients had associated comorbidities, the cardiovascular diseases and risk factors being the most prevalent: dyslipidaemia 80%, hypertension 51.7%, obesity 34.2%, and cardiovascular events 34.2%.

Hyperuricemia and associated factors

Around a third of the patients (27.5%) had hyperuricemia. There were no differences in PsA patients with a high level of serum uric acid compared to the ones with normal levels with respect to demographic and clinical variables (Table 1). However, patients with hyperuricemia had a higher prevalence of cardiovascular comorbidities, namely obesity, hypertension, ischemic heart disease and diabetes (Table 1).

Hyperuricemia correlated only with cardiovascular comorbidities, including obesity (r=0.296, p=0.001), diabetes (r=0.221, p=0.015), ischemic heart disease (r=0.219, p=0.016) and hypertension (r=0.181, p=0.049), but not with moderate/severe skin psoriasis (r=0.016, p=0.862). The variables that were statistically significant associated to hyperuricemia in the univariate logistic regression and then included in the multivariate analysis were: obesity, hypertension, chronic kidney disease, diabetes and ischemic heart disease (Table 2). In the multivariate analysis, hyperuricemia was best explained by diabetes (odds ratio: 4.95, [95% confidence intervals: 1.47; 16.67]), ischemic heart disease (3.61 [1.00; 12.98]) and obesity (1.86 [1.04; 3.32]) (Table 2).

***TABLE 2**. Factors associated with hyperuricemia in psoriatic arthritis: univariate and multivariate logistic regressions*

Variable	Univariate analysis p value	Multivariate analysis OR [95% confidence interval] (p value)
Obesity	0.001	**1.86 [1.04; 3.32] (0.03)**
Hypertension	0.049	1.17 [0.42; 3.30] (0.76)
Chronic kidney disease	0.098	0.28 [0.03; 1.48] (0.12)
Diabetes mellitus	<0.001	**4.95 [1.47; 16.67] (0.01)**
Ischemic heart disease	0.016	**3.61 [1.00; 12.98] (0.05)**

For the multivariate analysis, significant results are in bold type

DISCUSSION

The study confirms that hyperuricemia is frequent in PsA, since almost a third of the patients had high levels of serum uric acid. Moreover, it was best explained by some of the cardiovascular comorbidities and not by the extent of the skin lesions.

Hyperuricemia occurred in 27.5% of the PsA patients, similar to previous studies (7). The prevalence is higher than in the general population where hyperuricemia is reported to occur in 5 to 13% (16). This is probably due to the association with the metabolic syndrome, which was demonstrated to be higher in PsA compared to the general population (1,5).

The factors that were associated with hyperuricemia in the current studies were mainly related to cardiovascular comorbidities; there was no relationship with the extent of the skin disease. These results are in concordance with previous studies. In psoriasis alone, hyperuricemia was also shown to have a higher prevalence than in the general population and to be associated with obesity and hypercholesterolemia rather than skin involvement (10,17). In psoriatic arthritis there was also no correlation between serum uric acid and psoriasis extent. In a Canadian cohort of PsA patients, hyperuricemia was associated with age, hypertension, ischemic heart disease, vasodilators, elevated serum creatinine and elevated serum total cholesterol (7); however body mass index/ obesity was not included. The best predictive model that explained hyperuricemia in PsA in this study included renal impairment, namely high levels of serum creatinine (odds ratio, OR 30.8, p<0.001) and hypercholesterolemia (OR 3.7, p<0.001) (7).

The current study has several limitations. Firstly, it included PsA patients from a tertiary centre which may lead to a selection of more severe cases. However, the patient and disease characteristics were as expected. Secondly, the cross-sectional design of the study does not allow identifying causal relationships, only associations. Lastly, is very difficult to have a standardized screening for comorbidities and risk factors in clinical practice. However, in the current study all PsA patients were screened for cardiovascular diseases.

In clinical practice is important to determine the level of serum uric acid in PsA patients, since high values might suggest a possible association with the metabolic syndrome, and therefore a screening for cardiovascular comorbidities should be done. In PsA there is a high prevalence of cardiovascular comor-

bidities, more than in the general population and psoriasis and similar to diabetes or rheumatoid arthritis (1,2,5,18). This is due to both traditional and non-traditional risk factors (1,2). The importance of cardiovascular screening in PsA is also supported by the EULAR recommendations for the management of cardiovascular in inflammatory arthritis (19). Furthermore, the evaluation of comorbidities including cardiovascular diseases was stated as an overarching principle in both EULAR and Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recommendations for management of PsA (20,21). Even in the absence of manifest cardiovascular diseases or risk factors, a special attention to these comorbidities is still needed, since hyperuricemia was shown to be correlated to subclinical atherosclerosis in PsA (2).

In conclusion, hyperuricemia in PsA is associated with metabolic syndrome rather than skin disease, but further longitudinal studies are needed to identify causal relationships.

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